UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte ACHIM BERTHOLD, WALTER MÜLLER, and GIOVANNI GAVIRAGHI

Appeal 2006-3007
Application 10/031,529
Technology Center 1600

ON BRIEF

Before ADAMS, GRIMES, and LEBOVITZ, *Administrative Patent Judges.*

GRIMES, *Administrative Patent Judge.*

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a transdermal patch. The Examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

BACKGROUND

Calcium antagonists of the dihydropyridine type include nifedipine and nilvadipine (Specification, page 1). They are used to treat hypertension (*id.* at 2, lines 19-22).

The specification discloses a transdermal therapeutic system for administering dihydropyridine-type calcium antagonists. The system includes a backing layer, a "drug reservoir containing a solution comprising a calcium antagonist and at least one skin permeation enhancer," a membrane to control release of the active agent, and an adhesive layer (*id.* at 2, ll. 9-15). "The solution comprising a calcium antagonist . . . and at least one skin permeation enhancer may be in a liquid, semisolid or thixotropic form" (*id.* at 3, ll. 17-18).

"Examples of suitable skin permeation enhancers . . . include saturated and unsaturated fatty acid esters, alcohols such as ethanol, propanol, isopropanol, n-decyl alcohol, etc[.], pyrrolidone derivatives (i.e. N-methyl-2-pyrrolidone)" (*id.* at 3, ll. 28-30).

DISCUSSION

1. CLAIMS

Claims 13-23 are pending and on appeal. The claims have not been argued separately and therefore stand or fall together. 37 CFR § 41.37(c)(1)(vii). Claims 13, 14, and 19 are representative and read as follows:

13. A transdermal therapeutic system for administering a calcium antagonist of the dihydropyridine type which comprises:

a) a backing layer, which defines the upper surface of the device,

b) a drug reservoir containing a solution comprising:
- a calcium antagonist of the dihydropyridine type,
- an alcohol selected from the group consisting of ethanol, propanol, isopropanol, and n-decyl alcohol,
- a pyrrolidone derivative, and

- a saturated or unsaturated fatty acid ester of a carboxylic acid containing 8 – 16 carbon atoms and polyhydroxy alcohol,

c) a membrane to control the release of the active ingredient, and

d) a pressure sensitive adhesive layer for attaching the system to the skin and,

if necessary, a release liner on the outer face of the adhesive layer

wherein the said backing layer and said membrane are connected together to form the drug reservoir.

14. A transdermal therapeutic system as claimed in claim 13 wherein the solution in the drug reservoir comprises a calcium antagonist of the dihydropyridine type, ethanol, N-methyl-2-pyrrolidinone [sic] and sorbitan palmitate.

19. A transdermal therapeutic system as claimed in claim [13] in which the calcium antagonist of the dihydropyridine type is nifedipine.

Claim 13 is directed to a transdermal patch comprising a backing layer, drug reservoir, release-controlling membrane, and adhesive layer. The drug reservoir contains a solution that comprises a dihydropyridine-type antagonist and three permeation enhancers: an alcohol (e.g., ethanol), a pyrrolidone derivative, and a fatty acid ester of a C_8-C_{16} carboxylic acid and a polyhydroxy alcohol.

Claim 14 specifies that the permeation enhancers are ethanol, N-methyl-2-pyrrolidone, and sorbitan palmitate. Claim 19 specifies that the calcium antagonist is nifedipine.

2. OBVIOUSNESS

Claims 13-23 stand rejected under 35 U.S.C. § 103 as obvious in view of Ueda[1] and Konno.[2] The Examiner reasons that Ueda teaches a patch that "comprises nilvadipine . . . , unsaturated fatty acid, and pyrrolidone derivative (col. 2, lines 45-61; col. 4, lines 49-50; examples)" (Examiner's Answer, pages 3-4). The Examiner relies on Konno for its disclosure of a "patch comprising a solution comprising the drug and penetration enhancer, such as sorbitan middle chain fatty acid ester (abstract; col. 3, lines 13-15). Drugs suitable for delivery by those patches include nicardipine and nifedipine dissolved in ethanol, N-methyl-2-pyrrolidone or mixture thereof (col. 2, lines 33-34; . . . 49-58)" (*id.* at 4).

The Examiner concluded that the claimed transdermal delivery system would have been obvious in view of the cited references (*id.* at 4-5). We agree. Ueda teaches a transdermal delivery system for administering nilvadipine (col. 1, l. 44). The system comprises a support member (i.e., backing), a release-controlling film, and an adhesive layer (col. 4, ll. 10-18).

Ueda teaches that "ethanol and/or an unsaturated higher fatty acid can markedly promote the percutaneous absorption of the dihydropyridine compound" (col. 1, ll. 59-61). Ueda also teaches that the composition optionally contains other percutaneous absorption promoters, including fatty acid esters, mono-, di- or triglycerides, and "pyrrolidone and derivatives thereof" (col. 2, ll. 52-61).

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[1] Ueda et al., U.S. Patent 5,045,553, issued Sept. 3, 1991.
[2] Konno et al., U.S. Patent 4,879,119, issued Nov. 7, 1989.

Like Ueda, Konno teaches a transdermal delivery system useful for delivering dihydropyridine-type calcium antagonists (col. 2, l. 34). The system comprises "a vegetable saturated fatty acid having 12 to 18 carbon atoms as a base together with a penetration enhancer" (col. 1, ll. 36-37). Konno teaches that "a mixed solvent of, for example, N-methyl-2-pyrrolidone and propylene glycol is suitably used for nifedipine" (col. 2, l. 67 to col. 3, l. 1). Konno also teaches that "sorbitan middle chain fatty acid ester" is an appropriate penetration enhancer (col. 3, l. 14).

We agree with the Examiner that these teachings would have made obvious the products of the instant claims. With respect to claim 13, Ueda discloses all of the components recited in the claims with the exception of the fatty acid ester. Konno teaches that sorbitan middle chain fatty acid ester is a penetration enhancer suitable for use with dihydropyridine-type calcium antagonists. Those of ordinary skill in the art would have found it obvious to include the sorbitan fatty acid ester in Ueda's system because Ueda suggests including more than one penetration enhancer in the disclosed composition (col. 2, ll. 52-61). A "middle chain fatty acid ester" reasonably appears to encompass fatty acid esters with 8-16 carbons.

With respect to claim 19, it would have been obvious to substitute nifedipine for Ueda's nilvadipine because Konno teaches that nifedipine is appropriate to administer transdermally.

With respect to claim 14, Ueda discloses all of the recited elements except sorbitan palmitate and N-methyl-2-pyrrolidone. Konno suggests that a mixed solvent of N-methyl-2-pyrrolidone and propylene glycol is suitable for nifedipine; thus, those skilled in the art would have found it obvious to

use this solvent for, at least, nifedipine. Konno also teaches that sorbitan middle chain fatty acid ester is a suitable penetration enhancer. This disclosure would have suggested sorbitan palmitate to those of ordinary skill in the art since a "middle chain fatty acid" would reasonably suggest a fatty acid with sixteen carbons (i.e., palmitic acid).

Appellants argue that Ueda does not disclose a pharmaceutical composition in solution form but only in the "form[ ] of gels containing a dihydropyridine compound with ethanol and/or an unsaturated higher fatty acid" (Br. 6-7).

This argument is unpersuasive. Ueda discloses "solution gels" made by gelling different solutions using hydroxypropylcellulose-H. See column 3, lines 5-20 and Examples 3, 7, 8, and 10. The instant specification states that a "solution . . . may be in a liquid, semisolid or thixotropic form" (page 3, ll. 17-18, emphasis added). Therefore, the "solution" recited in the claims reads on the "solution gel" disclosed by Ueda.

With respect to claim 14, Appellants argue that "sorbitan palmitate . . . is not encompassed by the 'unsaturated higher fatty acid esters' used in Ueda . . . and is not encompassed by the triglyceride fatty acids or permeation enhancers described in Konno." (Br. 8.)

We also find this argument unpersuasive. As discussed above, the permeation enhancers disclosed by Konno include "sorbitan middle chain fatty acid esters." This disclosure encompasses, and would have suggested to those skilled in the art, sorbitan palmitate. Appellants have provided no evidence or sound reasoning to support a contrary conclusion.

Finally, Appellants argue that the references do not support the rejection of claims 18 and 19 because the Examiner has not established that it would have been obvious to substitute one dihydropyridine-type calcium antagonist (e.g. nifedipine) for another (e.g., nilvadipine). (Br. 9.)

This argument is also unpersuasive. Ueda and Konno both teach transdermal delivery systems for administering dihydropyridine-type calcium antagonists. Ueda's system is disclosed specifically for nilvadipine, but Konno teaches that a variety of other drugs are appropriate for transdermal delivery, including nifedipine. Those of skill in the art would reasonably have expected Ueda's system to be suitable for delivering dihydropyridine-type calcium antagonists other than nilvadipine, including the nifedipine that Konno suggests administering transdermally. We therefore agree with the Examiner that it would have been obvious to combine the teachings of the cited references.

We have considered the other arguments in the Appeal Brief. They are adequately addressed above.

SUMMARY

The references relied on by the Examiner would have suggested the products of claims 13, 14, and 19 to those of ordinary skill in the art. We therefore affirm the rejection of those claims under 35 U.S.C. § 103. Claims 16, 17, 20, 21, and 23 fall with claim 13; claims 15 and 22 fall with claim 14; and claim 18 falls with claim 19.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Donald E. Adams)
Administrative Patent Judge)
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Eric Grimes)
Administrative Patent Judge) APPEALS AND
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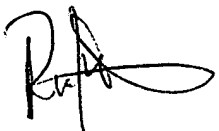
) INTERFERENCES
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